REMARKS

With entry of the current amendment, claims 8-12 have been cancelled. Claims 13-31 are withdrawn by the Examiner as drawn to a non-elected invention. Therefore, claims 1-7 are currently under examination.

Claims 1 has been amended to recite a heterologous nucleic acid molecule comprising a fusion polynucleotide comprising a sequence encoding a polypeptide sequence of interest linked to a reporter sequence. This amendment adds no new matter and is fully supported throughout the specification and claims as filed.

The rejections will be addressed in the order presented in the Office Action mailed October 11, 2002.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 8-12 were rejected as allegedly not enabled. Claims 8-12 each depend from claim 1. These dependent claims recite a mechanism relating to homologous recombination. However, the recited mechanisms do not limit the scope of claim 1. Accordingly, the claims are not proper dependent claims. Applicants have therefore cancelled claims 8-12. Thus, the rejection is moot.

Rejections under 35 U.S.C. § 103

Claims 1-10 and 12 stand rejected as allegedly obvious over Swoboda *et al.*, in view of Lyznik *et al.* Claims 1-10 and 12 are also rejected as allegedly unpatentable over Swoboda *et al.*, in view of Lyznik *et al.* and further in view of Ow *et al.* Lastly, claims 1-4 and 7-12 are rejected as allegedly obvious over Swoboda *et al.* in view of Lyznik *et al.* and further in view of Miao *et al.* Applicants respectfully traverse. Not only do the cited references fail to disclose each element of the claimed invention, but the Examiner has also failed to provide the required motivation to combine references. Indeed, the Examiner's proposed modifications of Swoboda *et al.* render the prior art invention unsatisfactory for its intended purpose. Moreover, assuming *arguendo* that such modifications could successfully be made, the proposed modifications change

the principle of operation of the reference. Therefore, as explained below, there can be no motivation to modify the homologous recombination system taught by Swaboda *et al.* Accordingly, the invention is not obvious.

The Examiner's proposed modifications render the homologous recombination system taught in Swoboda *et al.* inoperable

The MPEP (§ 2143.01) is clear that a modification proposed in an obviousness rejection must not make the prior art invention unsuitable. If proposed modifications would render the prior art invention being modified unsatisfactory for its intended purpose, there is no suggestion or motivation to make the proposed modification *In re Gordon, 733F.2d 900, 221 USPQ 1124 (Fed. Cir. 1984).*

The Examiner alleges that Lyznik *et al.* teach the advantage of a promoterless construct for recombination and that one of skill would have been motivated to redesign Swoboda *et al.* to include a promoterless construct. In the Swoboda *et al.* system, overlapping deletions of the GUS gene, which are each individually incapable of generating a β-glucuronidase signal, were incorporated into a recombination substrate plasmid. Upon recombination, a functional β-glucuronidase gene is restored and the product can be detected by hisochemical staining. The deletion genes flank a hygromycin resistance gene, which is used to initially select plants that take up the plasmid vector. The recombination marker generated by a homologous recombination event consists of a chimeric *uidA* gene driven by the 35 S promoter of cauliflower mosaic virus (CaMV). This promoter, which is introduced into the plant via the recombination vector, is active in all plant tissues. The *uidA* gene includes the translation start site and first 29 amino acids of the ORF V of CaMV fused to the bacterial *uidA* gene. Inclusion of the eukaryotic sequences results in stronger expression relative to the wildtype GUS gene. Swoboda *et al.* state that "[t]his strong and tissue unspecific expression was a prerequisite for the detection of recombination events in our whole plant assay system" (page 485, column 2, first paragraph, sentence five).

The Examiner argues that the practitioner would have been motivated to modify the recombination system described by Swoboda *et al.* to have a promoterless construct, *i.e.*, the Examiner argues that, like the claimed invention, the recombination substrate in Swoboda that is introduced into the plants cells can be modified to lack regulatory sequences. However, this will not satisfy Swoboda's requirement for strong and tissue unspecific expression. Thus, the Examiner's proposed modification renders the invention disclosed in Swoboda *et al.* unsatisfactory for its intended purpose. Therefore, in accordance with MPEP §2143.01, there is no suggestion or motivation to make the proposed modification.

A combination of prior art cannot change the principle of operation of the prior art invention

Additionally, a proposed modification cannot change the principle of operation of a reference (MPEP §2143.01). If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the reference are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.d2 810, 123 USpQ349 (CCPA 1959).

In order for the Examiner's modification of Swoboda *et al.* (in view of Lyznik *et al.*) to arrive at the claimed invention, it would require substantial redesigning *i.e.*, the operation of the prior art system itself would need to be altered. As explained above, the recombination system of Swoboda *et al.* relies on reconstitution of a functional reporter gene from two deletion mutants to detect homologous recombination. These deletion mutants are engineered into a vector, *i.e.*, a recombination substrate, which is in turn introduced into the plant. (Applicants note that the fused ORF V amino acid sequence is unrelated to the homologous recombination event). In order to arrive at the claimed invention, the operation of the system would have to change.

In the current invention, recombination occurs between the region of the nucleic acid molecule that comprises the targeting sequence, that is the sequence that encodes the polypeptide of interest, and DNA in the plant cell. In Swaboda *et al.*,

recombination occurs between the mutant genes, both of which are incorporated in the plasmid introduced into the plant. Further, the operative principle for detecting recombination in Swaboda *et al.* relies on reconstitution of a functional reporter from the two mutant forms. In the current invention, homologous recombination is detected as a result of reporter activation via the presence of the regulatory sequences present in the plant DNA. There is no mutant, inactive form of the reporter. Clearly, modifications to Swaboda *et al.* that are suggested by the Examiner would necessitate the substantial redesign of Swaboda *et al.* and change the principles underlying the design of the system.

Similarly, Lyznik *et al.* cannot be modified or combined with Swaboda *et al.* without altering the principle of operation. Lynik *et al.* teach a transient system that detects recombination events that occur between two plasmids introduced into a plant protoplast. The system does not identify recombination between introduced DNA and plant DNA. Modification of this system to incorporate the features of the claimed invention would clearly change the principle in which the detection system of Lyznik *et al.* works.

Thus, the changes to Swaboda *et al.* or Lyznik *et al.* required to make the claimed invention cannot be made without changing the basic principles under which the prior art systems were designed to operate. Accordingly, the teachings of the cited art do not support a case of obviousness (*See, e.g., In re Ratti, supra*).

The cited art does not disclose all of the elements.

Lastly, Applicants reiterate that Swoboda *et al.* and Lyznik *et al.* do not disclose all of the elements of the claims. The instant claims recite a heterologous nucleic acid molecule comprising a fusion polynucleotide comprising a sequence encoding a polypeptide sequence of interest linked to a reporter sequence. The region of the fusion polynucleotide that encodes the polypeptide sequence of interest targets the construct to a plant gene. Swoboda *et al.* teach a nucleic acid encoding a region of CaMV ORF V fused to GUS. CaMV ORF V does not target the construct to a plant gene. Lyznik *et al.* teach a construct that has an intron linked to sequences encoding a

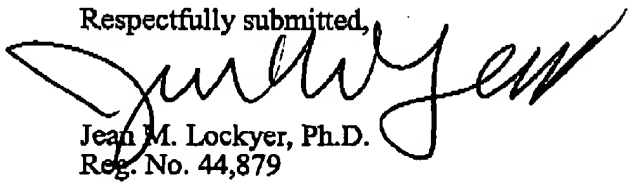
reporter gene. The intron does not target the sequence to plant DNA. Thus, the references do not disclose all of the elements of the claims.

In light of the above, the claimed invention is not obvious over the cited art. Applicants therefore respectfully request withdrawal of the rejection.

The rejections of the claims further in view of Miao *et al.* and/or Ow *et al.* are also traversed. The combination of primary references is defective for the reasons noted above. The secondary references do not cure the defects. Thus, the rejection fails to establish a proper case of obviousness. Applicants therefore respectfully request their withdrawal.

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 415-576-0200.

Respectfully submitted,



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